REMARKS

Claims Pending in the application:

Claims 1,3, and 36-50 remain pending in this response.

Claim Numbering:

Applicants' note the Examiner's renumbering of the claims due to missing claim 32.

Examiner's Utility/Enablement Rejection

Claims 1, 3, and 35-49 are rejected as allegedly lacking support by either a specific asserted utility or a well established utility. Applicants respectfully traverse this rejection.

As disclosed in the specification and in the prior response, oncogenes such as Wnt-1 are genes that when mis-regulated are linked to cancer. "Wnt expression, such as overexpression, represents attractive therapeutic targets to treat cancer." (page 1, Paragraph 0004, *citing* Pennica et al., 1998). *In vivo*, Wnt expression leads to mammary tumors in transgenic mice (Tsukamoto et al., 1988). When Wnt-1 is overexpressed in mouse mammary tissue, cells are partially transformed. "In this in vitro model, genes that are differentially regulated by Wnt-1 overexpression, when compared to wild-type or non-transforming Wnt-4-expressing cells, represent candidate genes that are involved in tumorgenic processes. (*Id.*) Wnt family members are cysteine-rich, glycosylated signaling proteins that mediate diverse developmental processes, such as the control of cell proliferation, adhesion, cell polarity, and the establishment of cell fates. (page 1, lines 7-11).

In an *in vitro* model of retinoic acid (RA)-induced cellular differentiation, mSTRA6 was identified as being upregulated. mSTRA6 codes for a very hydrophobic membrane protein. Studies have shown mSTRA6 to be an important molecule in cellular proliferation and differentiation. See, for example, Chazaud et al., 1996. Accordingly, Applicants submit Wnt induced upregulated mSTRA6 was understood at the time of the present invention to be a candidate gene involved in the tumorgenic process.

The inventors have identified an important downstream cellular component of the Wnt-1 signaling pathway in mammary cells transformed by Wnt-1, solving the problem of downstream Wnt-1 targets. Using the Wnt-1 expressing C57MG mouse mammary epithelial cell model, STRA6 was identified as an upregulated gene. These results were confirmed in a QEA analysis, that demonstrated upregulation of STRA6 in Wnt-1 epressing cells (11-fold higher than wild-type or Wnt-4 expressing cells). This showing of differential expression regulated by Wnt-1 expression, demonstrates STRA6 as a candidate gene for diagnosis and therapeutic use, particularly in cancer. A diagnostic assay based on differential expression of STRA6 as compared with a control is supported by the teachings of the specification. (page 1, lines 23-26; page 4, lines 20-25; page 15, lines 4-14).

The human STRA6-like (hSTRA6) polypeptide exhibits strong homology and sequence identity to the mSTRA6 protein (page 12, lines 2-14, Table 5). More than just homology is shared, structural and cell biological features are common to both mSTRA6 and hSTRA6. Both proteins localize to the cell membrane. Both have 7-8 membrane spanning domains (Fig. 1, page 14, lines 11-14).

For the reasons discussed above, Applicants submit the asserted diagnostic utility for hSTRA6 is specific, substantial, credible, and fully supported by the specification. An assertion of utility is credible unless the logic underlying the assertion is seriously flawed, or the facts upon which the assertion is based are inconsistent with the logic. No such showing has been made by the Examiner. The asserted utility is specific: hSTRA6 differential expression specifically relates to cellular transformation and cancer diagnosis. The asserted utility is substantial: cancer diagnosis is a substantial part of today's health concerns, as this serious illness claims many lives each day. In view of the specific, substantial, and credible disclosure provided by the specification, and the Examiner's failure to show any inconsistency or flaws in the asserted facts or logic, removal of this rejection is requested.

Applicants assert the requirements of § 101 are met. Because the specification meets the utility requirement, applicant asserts one of skill in the art would know how to make and use the

claimed invention, as taught by the specification. Withdrawal of the § 101 and § 112, 1st paragraph rejections is requested.

Written Description

Claims 1, 36-38, and 40-49 are rejected as allegedly lacking written description. Applicants respectfully traverse this rejection.

As discussed above for utility and enablement, and in the prior response, the specification provides sufficient teaching, correlations, and description of the claimed hSTRA6 and its use, for example in the diagnosis of cancer. Furthermore, Applicants disclose two peptide sequences of STRA6 and correlates the sequences to a known murine STRA6 sequence. One of skill in the art, following well known principles, would be under no undue burden to produce and use the claimed functional variants. A description is presumed to be adequate, unless sufficient evidence or reasoning to the contrary is presented. Compliance with the written description requirement does not require the subject matter to be exactly described, but requires a showing that one skilled in the art would recognize the applicant had invented what was claimed. (MPEP 2163.02).

Written description requires a precise definition by structure, formula...sufficient to distinguish the claimed invention from other materials. A formula is normally adequate. (*Univ. California v. Eli Lilly and Co.*, 43 USDQ 2d 1398, 1405 (Fed. Cir. 1997). Because the sequence of hSTRA6 is provided in Table 2 (SEQ ID NO:2) and 4 (SEQ ID NO:4) (pages 35-36), and variants of these are taught and also described by formula (page 20, lines 28-31), Applicants assert the claimed invention is adequately described. In view of this teaching in the specification, Applicants submit the claims are fully described in the specification. Removal of this rejection is requested.

New Matter

Claims 44 and 46 are rejected as lacking written description. Amendment of these claims renders the rejection moot. Removal is requested.

Anticipation

The Examiner has rejected claim 1 as anticipated by anyone of six references.

U.S. 2002 0156 52A1 dated 1/13/04

U.S. 20021703461A1 dated 1/13/04

U.S. 20030149239A1 dated 1997, 1998

U.S. 20030187201A1 dated 1997, 1998, 1999

U.S. 20030187202A1 dated 1997, 1998, 1999

U.S. 20030187203A1 dated 1997, 1998

In contrast to the Examiner's rejection, these references fail to disclose a sequence having at least 99% identity to SEQ ID NO: 2, as required by claim 1. In contrast, as shown in the Blast analysis provided by the Examiner, these references disclose a polypeptide having 2 amino acid changes, for example, having less than 99% identity. Removal of this rejection is requested.

In view of the above amendments and remarks, Applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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